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10/800,043

03/11/2004

Gary Opperman

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MERCHANT & GOULD PC  
P.O. BOX 2903  
MINNEAPOLIS, MN 55402-0903

EXAMINER

HILL, KEVIN KAI

ART UNIT

PAPER NUMBER

1633

MAIL DATE

DELIVERY MODE

10/18/2007

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

10/800,043

Applicant(s)

OPPERMAN ET AL.

Examiner

Kevin K. Hill, Ph.D.

Art Unit

1633

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 24 August 2007.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1, 3-6, 10-18, 21-65 is/are pending in the application.
- 4a) Of the above claim(s) 3-6, 22-41 and 46-62 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 10-18, 21, 42-45 and 63-65 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                 | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date: _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                        | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date: _____ | 6) <input type="checkbox"/> Other: _____  |

### **Detailed Action**

#### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 24, 2007 has been entered.

Applicant has elected the invention of Group I, Claims 1-21 and 42-45, drawn to a composition comprising a compound suitable for being immobilized on support and an organic anion of Formula I:  $R(X)_m(Y)_n$ , and a method of forming spots of said compound on a surface.

Within Group I, Applicant has further elected the restricted subgroup structure "b" of the organic anion of Formula I:  $R(X)_m(Y)_n$ , wherein the anion has the Formula III, specifically the organic anion composition to be phytate.

Election of Applicant's invention(s) was made without traverse. However, the species elections were traversed. Applicant argues that a search of both formulas and all possible moiety variables would not present a serious search burden.

### ***Amendments***

Applicant's response and amendments, filed July 30, 2007 to the prior Office Action is acknowledged. Applicant has cancelled Claims 2, 7-9, and 19-20, withdrawn Claims 3-6, 22-29, 31-41, 46-62, amended Claims 1, 10, 16-17 and 42-43, and added new claims, Claims 63-65. Applicant's new claims have been entered into the application as requested and will be examined on the merits herein, as they are considered to belong to the elected group. Support for the added claims has been found at page 12, lines 26-31 of the specification.

The Examiner notes that claim 30 is not similarly annotated as being withdrawn as indicated for other claims also dependent upon withdrawn base claim 22.

Claims 3-6, 22-41 and 46-62 are pending but withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a non-elected invention, there being no allowable generic or linking claim.

Claims 1, 10-18, 21, 42-45 and 63-65 are under consideration.

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### ***Priority***

Applicant makes no claim for benefit or priority of a prior-filed application. Accordingly, the effective priority date of the instant application is granted as the filing date of the instant application, March 11, 2004.

### ***Examiner's Note***

Unless otherwise indicated, previous objections/rejections that have been rendered moot in view of the amendment will not be reiterated. The arguments in the July 30, 2007 response will be addressed to the extent that they apply to current rejection(s).

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. **Claims 1 and 16 stand and claim 14 is newly rejected under 35 U.S.C. 102(b)** as being anticipated by Kretz (U.S. Patent No. 6,110,719).

This rejection is maintained for reasons of record in the office action mailed May 30, 2007 and re-stated below. The rejection has been re-worded slightly based upon Applicant's amendment filed July 30, 2007.

With respect to Claims 1 and 16, Kretz teaches a composition comprising sodium phytate in a Tris HCl buffer, pH 7.5 (column 3, lines 32-40). Kretz teaches that the composition comprises the phytase enzyme (column 3, line 33), wherein the instant specification discloses that compositions suitable for being immobilized on a support include biomolecules such as proteins (pg 12, lines 10-13 and 23-25).

With respect to the limitation that the compound suitable for being immobilized on a support be modified, while the specification discloses that the biomolecules may be modified, for example, by an amine group, a sulfhydryl group, or a mixture thereof (pg 12, lines 26-31), the specification does not exclude any particular form of modification. Kretz et al disclose that the phytase enzyme may be modified to further comprise additional amino acid sequences to impart desired characteristics or fused to another compound (col. 9, lines 27-35; col. 10, lines 24-37; col. 13, lines 20-24). Depending on the source organism from which the phytase is obtained, the phytase may be glycosylated or non-glycosylated (col. 14, lines 23-25).

With respect to the limitation that the phytate be effective to substantially decrease ring formation upon drying of a spot less than or equal to about 300 $\mu$ m diameter on a support, such a limitation is considered an inherent feature because the claim does not require a particular concentration or amount of phytate necessary and sufficient to achieved the claimed result. Absent evidence to the contrary, the buffer composition of Kretz et al comprising phytate inherently possesses the property of being effective to substantially decrease ring formation upon drying of a spot less than or equal to about 300 $\mu$ m diameter on a support.

With respect to claim 14, Kretz et al disclose that the art recognizes that phytase yields inorganic phosphate when it acts on phytate (col. 1, lines 50-52). Thus, the buffer composition of Kretz et al comprising phytate and phytase inherently possesses inorganic phosphate, absent evidence to the contrary.

Thus, Kretz anticipates Claims 1, 14 and 16.

#### ***Applicant's Arguments***

Applicant argues that the buffer composition of Kretz et al does not possess each and every element of the claims, specifically phytate and a modified compound suitable for being immobilized on a support.

Applicant's argument(s) has been fully considered, but is not persuasive. The art recognizes that an enormous genus of post-translational modifications of a polypeptide are known to exist in the cell, including phosphorylation, ubiquitination, attachment of acetyl or alkyl groups, biotin, sulfate, selenium, phosphopantethein, various isoprenoids, numerous lipids, diverse carbohydrates, changing the chemical structure of an amino acid (de-amination and de-amidation), or making structural changes such as peptide cleavage and di-sulfide bridges ([en.wikipedia.org/wiki/Posttranslational\\_modification](http://en.wikipedia.org/wiki/Posttranslational_modification), last visited January 18, 2007). Kretz et al disclose that the phytase enzyme may be modified, thus fulfilling the instant claims.

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. **Claims 1, 10-18 and 21 stand rejected under 35 U.S.C. 103(a)** as being unpatentable over Kreft et al (Eur. F. Physiol. 439(Suppl): R66-67, 2000), as evidenced by Alberts et al (*Molecular Biology of the Cell, Third Edition*, Garland Publishing, New York, NY, 1994, pg 58), and Veraart et al (J. Chromatography A, 768: 307-313, 1997).

This rejection is maintained for reasons of record in the office action mailed May 30, 2007 and re-stated below. The rejection has been re-worded slightly based upon Applicant's amendment filed July 30, 2007.

Kreft et al teach nucleic acid hybridization compositions comprising nucleic acids, e.g. DNA, RNA, or mixtures thereof, the compositions further comprising an anionic surfactant SDS, inorganic phosphate and sodium phosphate, pH 7.0, and/or inorganic surfactants extant in Denhardt's Solution (Materials and Methods, pgs 66-67, joining ¶).

With respect to the limitation that the compound suitable for being immobilized on a support be modified, while the specification discloses that the biomolecules may be modified, for example, by an amine group, a sulfhydryl group, or a mixture thereof (pg 12, lines 26-31), the specification does not exclude any particular form of modification. Kreft et al teach the use of digoxigenin-labelled RNA probes (pg R66, col. 2, Nonradioactive technique) for hybridization, thus fulfilling the limitation of a 'modified compound'.

With respect to the limitation that the modified compound comprise an amine group, the art (Alberts et al, pg 58) has long-recognized that the adenine, guanine and cytosine nucleosides comprises an amine group.

Kreft et al do not teach the composition(s) to comprise phytic acid; however, at the time of the invention, Veraart et al taught the use of phytic acid with a pH buffer comprising inorganic phosphate at pH 7.5 (pg 308, column 2, ¶2.4.1). Veraart et al taught that phytic acid is a large, polyionic molecule whose ionic strength is relatively large as compared with its concentration (pg 307, column 2, lines 7-11).

Veraart et al do not teach that phytic acid will be effective to substantially decrease ring formation upon drying of a spot less than or equal to about 300 micrometer diameter on a support, as recited in Claim 1. However, it is understood that the recited property is an inherent

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property of phytic acid, not a structural limitation, and thus the composition of Kreft et al, modified by including phytic acid as taught by Veraart et al, would have the recited effects.

It would have been obvious to one of ordinary skill in the art to modify the hybridization buffer of Kreft et al with the phytic acid of Veraart et al with a reasonable chance of success because the art recognized the growing popularity of phytic acid as a buffering agent (see Abstract, line 1). All the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. An artisan would be motivated to include phytic acid in a nucleic acid hybridization composition because phytic acid has a relatively large ionic strength as compared with its concentration (pg 307, column 2, lines 7-11), and the art recognizes that increasing ionic strength can reduce non-specific adsorption to a support (pg 307, column 1). The availability of twelve acidic groups with pKa values ranging from 1.9-9.5 provides the possibility to use phytic acid not only as an additive to suppress wall adsorption effects, but also to control the pH (pg 308, column 1, lines 4-8). Furthermore, the decreased adsorption properties afforded by phytic acid would increase the specific hybridization signal to noise ratio, and thus would be advantageous in hybridization assays.

Thus, the invention as a whole is *prima facie* obvious.

### *Applicant's Arguments*

Applicant argues that neither Kreft et al nor Veraart et al teach or even suggest the addition of a modified compound that is suitable for immobilization on a support. Thus, the combined teaching of the references fails to disclose each and every element of the claims.

Applicant's argument(s) has been fully considered, but is not persuasive. Kreft et al teach the modification of nucleic acids with digoxigenin, thereby fulfilling the instant limitations.

6. **Claims 1 and 14-15 stand rejected under 35 U.S.C. 103(a)** as being unpatentable over Kretz (U.S. Patent No. 6,110,719) and Sambrook et al (Molecular Cloning: A Laboratory Manual, Second Edition, Cold Spring Harbor Laboratory Press, 1989).

This rejection is maintained for reasons of record in the office action mailed May 30, 2007 and re-stated below. The rejection has been re-worded slightly based upon Applicant's amendment filed July 30, 2007.

Kretz teaches a composition comprising sodium phytate in a Tris HCl buffer, pH 7.5 (column 3, lines 32-40). Kretz teaches that the composition comprises the phytase enzyme (column 3, line 33), wherein the instant specification discloses that compositions suitable for being immobilized on a support include biomolecules such as proteins (pg 12, lines 10-13 and 23-25).

With respect to the limitation that the compound suitable for being immobilized on a support be modified, while the specification discloses that the biomolecules may be modified, for

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example, by an amine group, a sulfhydryl group, or a mixture thereof (pg 12, lines 26-31), the specification does not exclude any particular form of modification. Kretz et al disclose that the phytase enzyme may be modified to further comprise additional amino acid sequences to impart desired characteristics or fused to another compound (col. 9, lines 27-35; col. 10, lines 24-37; col. 13, lines 20-24). Depending on the source organism from which the phytase is obtained, the phytase may be glycosylated or non-glycosylated (col. 14, lines 23-25).

With respect to the limitation that the phytate be effective to substantially decrease ring formation upon drying of a spot less than or equal to about 300 $\mu$ m diameter on a support, such a limitation is considered an inherent feature because the claim does not require a particular concentration or amount of phytate necessary and sufficient to achieved the claimed result. Absent evidence to the contrary, the buffer composition of Kretz et al comprising phytate inherently possesses the property of being effective to substantially decrease ring formation upon drying of a spot less than or equal to about 300 $\mu$ m diameter on a support.

Kretz et al disclose that the art recognizes that phytase yields inorganic phosphate when it acts on phytate (col. 1, lines 50-52). Thus, the buffer composition of Kretz et al comprising phytate and phytase inherently possesses inorganic phosphate, absent evidence to the contrary.

Kretz does not teach the composition to comprise about 10 to about 200mM sodium or potassium phosphate at pH of about 7 to about 10; however, at the time of the invention, Sambrook et al taught how an artisan may create phosphate buffered solutions using sodium phosphate and/or potassium phosphate (pg B.21, Tables B.10 and B.11; see also pg B.12 for recipe).

It would have been obvious to one of ordinary skill in the art to modify the buffer of Kretz with the inorganic phosphate-providing buffer of Sambrook et al with a reasonable chance of success because Sambrook et al teach how to make a phosphate buffer with a buffering capacity at pH 7.5. All the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. An artisan would be motivated to substitute the Tris-HCl buffer of Kretz with the phosphate buffer of Sambrook et al because the phosphate buffer would provide a greater amount of inorganic phosphate groups into the composition and enhance the activity and buffering capacity of the phytic acid.

Thus, the invention as a whole is *prima facie* obvious.



*Applicant's Arguments*

Applicant argues that Kretz does not teach or suggest modifying the phytase composition as required by claim 1, nor teach or suggest the addition of any other modified compound.

Applicant's argument(s) has been fully considered, but is not persuasive. As discussed above, the art recognizes that an enormous genus of post-translational modifications of a polypeptide are known to exist in the cell, including phosphorylation, ubiquitination, attachment of acetyl or alkyl groups, biotin, sulfate, selenium, phosphopantethein, various isoprenoids, numerous lipids, diverse carbohydrates, changing the chemical structure of an amino acid (de-amination and de-amidation), or making structural changes such as peptide cleavage and disulfide bridges ([en.wikipedia.org/wiki/Posttranslational\\_modification](http://en.wikipedia.org/wiki/Posttranslational_modification), last visited January 18, 2007). Kretz et al disclose that the phytase enzyme may be modified, thus fulfilling the instant claims.

In response to applicant's argument that Kretz does not teach or suggest modifying the phytase composition as required by claim 1, the reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. >See, e.g., *In re Kahn*, 441 F.3d 977, 987, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006)

7. **Claims 42-44 and 65 are rejected under 35 U.S.C. 103(a)** as being unpatentable over Guo et al (Genome Res. 12(3):447-457, 2002) and Veraart et al (J. Chromatography A, 768: 307-313, 1997).

Guo et al teach a method of forming spots of a compound on a surface, the method comprising applying to the surface, specifically activated glass slides, a composition comprising a modified compound, specifically oligonucleotides modified at the 5' end with an amino group, suitable for being immobilized on the surface, and forming a spot on the surface (pg 456, col. 1, Preparation of Oligonucleotide Arrays).

Guo et al do not teach the use of phytate. However, at the time of the invention, Veraart et al taught the use of phytic acid with a pH buffer comprising inorganic phosphate at pH 7.5 (pg 308, column 2, ¶2.4.1). Veraart et al taught that phytic acid is a large, polyionic molecule whose

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ionic strength is relatively large as compared with its concentration (pg 307, column 2, lines 7-11).

Neither Guo et al or Veraart et al teach that the buffer, specifically comprising phytic acid, will be effective to substantially decrease ring formation upon drying of a spot less than or equal to about 300 micrometer diameter on a support, as recited in Claim 42. However, it is understood that the recited property is an inherent property of phytic acid, not a structural limitation, and thus the method and buffer of Guo et al, modified by including phytic acid as taught by Veraart et al, would have the recited effect.

An artisan would be motivated to include phytic acid in a method of spotting organic compositions such as nucleic acids because phytic acid has a relatively large ionic strength as compared with its concentration (Veraart et al; pg 307, column 2, lines 7-11), and the art recognizes that increasing ionic strength can reduce non-specific adsorption to a support (Veraart et al; pg 307, column 1). The availability of twelve acidic groups with pKa values ranging from 1.9-9.5 provides the possibility to use phytic acid not only as an additive to suppress wall adsorption effects, but also to control the pH (Veraart et al; pg 308, column 1, lines 4-8). Furthermore, large, polyionic molecules are preferable because they provide high ionic strengths at relatively low currents (Veraart et al; pg 307, joining ¶). With relatively small ions used to enhance the ionic strength, the associated increment of the electric current is rather dramatic, resulting in the Joule heating effect. The Joule heating effect extant in piezoelectric delivery devices would be minimized in the presence of phytic acid, thus minimizing or avoiding unwanted heating of the composition that is to be deposited onto the support.

Thus, the invention as a whole is *prima facie* obvious.

8. **Claims 42 and 65 are rejected under 35 U.S.C. 103(a)** as being unpatentable over Guo et al (Genome Res. 12(3):447-457, 2002) and Veraart et al (J. Chromatography A, 768: 307-313, 1997), as applied to claims 42-44 and 65 above, and in further view of Rogers et al (Analytical Biochem. 266: 23-30, 1999).

The prior cited art does not teach the modified compound to comprise a sulfhydryl group. However, at the time of the invention, Rogers et al taught the sulfur modification of

oligonucleotides for the purpose of attaching the oligonucleotides to a surface (pg 24, col. 2, Immobilization).

It would have been obvious to one of ordinary skill in the art to substitute an amine group for a sulfhydryl group when modifying a composition to be immobilized on a surface with a reasonable chance of success because the art has long-recognized the ability to chemically modify a compound to enhance attachment of the compound to a surface and the simple substitution of one known, equivalent element for another would have yielded predictable results to one of ordinary skill in the art at the time of the invention. The attachment of nucleic acid probes most often occurs by their 5' termini, which must be amino or thiol-modified, depending on the chemical reactive group of the linker. Thus, the addition of an amino group, thiol group, or a mixture thereof each solves the same problem in the art.

Thus, the invention as a whole is *prima facie* obvious.

9. **Claims 42 and 45 are rejected under 35 U.S.C. 103(a)** as being unpatentable over Guo et al (Genome Res. 12(3):447-457, 2002), Veraart et al (J. Chromatography A, 768: 307-313, 1997) and Rogers et al (Analytical Biochem. 266: 23-30, 1999), as applied to claims 42-44 and 65 above, and in further view of Lemieux et al (\* of record in IDS).

The prior cited art does not teach the method of forming spots, wherein the applying step comprises pin or piezoelectric spotting. However, at the time of the invention, Lemieux et al summarized DNA chip-making technologies, stating that one may produce microarrays by mechanical microspotting by pins (pg 281, column 2, ¶1) or by ink-jet nozzles that rely on the piezoelectric effect (pg 281, column 2, ¶4).

It would have been obvious to one of ordinary skill in the art to substitute spotting method used by Guo et al with spotting methods using a pin or piezoelectric effect as taught by Lemieux et al with a reasonable chance of success because the art recognized that such technology was available at the time. All the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

Thus, the invention as a whole is *prima facie* obvious.

### *Conclusions*

10. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kevin K. Hill, Ph.D. whose telephone number is 571-272-8036. The examiner can normally be reached on Monday through Friday, between 9:00am-6:00pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph T. Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

*Kevin K. Hill*

*[Signature]*  
**Q. JANICE LI, M.D.**  
**PRIMARY EXAMINER**